

Exhibit C

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Re: United States of America ex rel. Ven-a-Care of the Florida Keys, Inc. v. Dey, Inc., et al., No. 05-11084-PBS

Dear Ms. Reid,

On February 5, 2010, plaintiffs' expert Dr. Mark Duggan submitted a letter showing "confidence interval" calculations for his extrapolated Medicaid federal "DIFFERENCES". I find that these new calculations presented by Dr. Duggan suffer from several conceptual and methodological flaws. Thus, Dr. Duggan's "confidence intervals" are unreliable and do not provide any additional support for his extrapolated differences. In summary:

- Actual claims data directly reveal the error rate in Dr. Duggan's extrapolations – bypassing the need for any "confidence intervals"
- There is no sound statistical basis for "confidence intervals" as calculated by Dr. Duggan
- Finally, Dr. Duggan has made calculation errors that underestimate his confidence intervals. Correcting only some of these errors doubles the margin of error around his extrapolation to +/- 17%

I elaborate on each of these observations below. I reserve the right to update my analysis if additional information becomes available. In addition, I reserve the right to supplement or modify my opinions, if warranted, and to prepare additional supporting materials, such as summaries, graphical exhibits, or charts.

1. Actual claims data directly reveal the error rate in Dr. Duggan's extrapolations

As I have previously noted, the error rate in Dr. Duggan's extrapolated differences can be assessed directly using actual claims data.¹ When the actual data are available, then this should be the benchmark against which extrapolations are tested and error rates assessed.²

In his November 30, 2009 letter to plaintiff counsel Dr. Duggan examined claims data for an additional 16 states that makes a comparison between his extrapolation and actual data possible. In that instance he arrived at a lower calculated difference than his extrapolation rendered. In particular, the supporting materials behind Dr. Duggan's letter showed that

¹ In this letter I am taking Dr Duggan's difference calculations as given in order to examine the issues associated with his extrapolation. As I have discussed in my initial reports, Dr. Duggan's difference calculations to begin with are based on flawed premises and lack economic rationale as damages.

² Using Dr. Duggan's confidence intervals to assess his difference extrapolations is like assessing how well one predicted yesterday's weather without having looked out the window. While it can be useful to attempt to assess one's confidence extrapolations absent actual data, once actual data is available it becomes the standard for assessing performance.

for the 16 additional states where claims data were available, he calculated differences of \$19.8 million. Dr. Duggan's extrapolated differences for these states had previously been \$22.1 million. Thus, Dr. Duggan's November 30th calculations revealed an upward error of more than 10% in his original extrapolations. This demonstrates that his estimates are likely biased – which as I will demonstrate below implies that he cannot construct a confidence interval; however, one cannot simply take this number as a bias correction factor.

It is important to recognize that these average differences mask considerable errors in Dr. Duggan's state-level difference calculations for Dey's drugs. Compared to calculations from the actual claims data for the 16 states, Dr. Duggan's extrapolation errs by more than 50% for some states. As I discuss in detail in my expert report, there is wide variation in Medicaid reimbursement levels across states driven by economic considerations and active policy choices. This variation is not random.

Dr. Duggan presents an entirely new regression model in his February 5 letter that underscores the importance of this state-level reimbursement variation for Dey's drugs. While Dr. Duggan does not discuss this model in his letter, the results can be found in his workpapers. His initial regression model, which essentially reproduces his extrapolation method, only explains about 30% of the variation in differences found in the actual data ($R^2 = 0.3061$). When he adds indicator variables that capture average differences from state to state (not part of his extrapolation) they are statistically significant and his R^2 jumps to 0.63. In essence, simple state-level effects appear to explain more variation in actual differences than was explained by the year-quarter-NDC averages Dr. Duggan uses for extrapolation.³ As Dr. Duggan himself concludes from his Abbott regression results, "there is systematic variation across states".⁴ This result is only more pronounced for Dey.

Hence as a methodological matter, extrapolations that do not take into account these systematic state variations are not likely to be reliable. Dr. Duggan's "confidence interval" calculations do not address this issue and hence provides no additional support for his extrapolations.

2. No statistical basis for confidence intervals as implemented by Dr. Duggan:

Dr. Duggan admits that the sample of states for which he calculated differences using claims data is not random.⁵ Using such a non-random sample of states, he has mechanically extrapolated differences for the remaining states. However, one cannot straight forwardly extrapolate from a non-random sample and doing so may result in arbitrary errors and unknown biases. In the presence of unknown statistical bias, the confidence interval calculation that Dr. Duggan performs is meaningless and does not have the standard interpretation that he incorrectly applies to it.

³ Dr. Duggan's state indicator variables likely underestimate the contribution of state policy decisions to reimbursement variation because they do not allow for changes in policy over time. Since changes to state-level policy over time – such as adoption of MAC or WAC – can have a particularly significant effect on generic drug reimbursement, this is likely to be a serious omission.

⁴ Duggan February 5, 2010 letter at 14.

⁵ See e.g. Abbott Daubert hearing on 1/22/10 at 214.

Some adjustment for the fact that the sample is not random is required. This is the underlying issue that Nobel Prize winning economist James Heckman explores in his seminal papers on sample selection bias (Heckman, 1978; Heckman, 1979). However, Dr. Duggan has not made any such corrections to his extrapolation, and his current approach is known (from Heckman and others) to be arbitrarily biased, and so may or may not turn out to be close to the actual differences. Thus, Dr. Duggan's current extrapolation is neither scientific nor statistically reliable.

In defense of his methodology, Dr. Duggan chooses to appeal to a study that produces estimates based upon non-random samples and make extrapolations.⁶ However, those authors also recognize the need to correct for the non-random nature of the sample:

“Our sample is not random, but it is rather selected by which practices chose to use the services of this particular vendor. To make our providers look more like the national population of doctors, we determined a weighting for each provider based on location, specialty, and practice size.”

Dr. Duggan has not made any such adjustments to his extrapolations to account for the non-random sample data he uses.⁷ As suggested by comparison to actual data above, Dr. Duggan's extrapolations are clearly not accurate and thus also likely to be biased. Given the likely bias of his estimates, there is no statistical basis to construct a meaningful confidence interval around his estimate. Certainly the “confidence interval” calculations he performs do not provide any reliable information regarding error rates.

3. Various errors in Dr. Duggan's calculation suggest margin of error of at least 17%

Even if the conceptual basis for Dr. Duggan's “confidence intervals” was sound, which it is not, his calculations nevertheless contain several errors that cause him to overstate the precision of his extrapolations. First, the program used by Dr. Duggan to calculate his standard deviation contains an error in coding that artificially deflates his standard deviation⁸. Second, in calculating the variance of his expression [7], Dr. Duggan crucially ignores the variation of the error term. This is a major conceptual error because one of the major bases for constructing a confidence interval for the true value arises from unexplained variations which Dr. Duggan has ignored. Third, Dr. Duggan assumes that “variables d_{snt} are uncorrelated”⁹ without providing any basis for it. Instead, one can relax this assumption and allow the variables d_{snt} to correlate.

⁶ Dr. Duggan had previously attempted to defend his ad-hoc extrapolation methodology by citing other articles and calculations. In my rebuttal report, I pointed out the flaws with those citations and calculations. See Bradford rebuttal at 13-15.

⁷ The simple adjustments applied by Gruber and Rodriguez are not likely to be the right ones in the current context. They merely illustrate – as argued by Dr. Heckman and many others – that some adjustment is necessary. However, proper adjustments may not even be possible in the current context.

⁸ Please refer to line 178 of Dr. Duggan's "02_34_states.do" file for a specific example of this error. Instead of calculating the average of a field that should be the same for all records (thus making the average the same value), Dr. Duggan's code takes the average of lower values that sum to the correct, larger value. By taking the arithmetic mean of these lower values Dr. Duggan depresses his standard deviation.

⁹ Duggan February 5, 2010 letter at 8.

Correcting the two errors identified above and relaxing the third assumption almost doubles Dr. Duggan's standard deviation estimate from \$2.508 million to \$5.12 million. Thus, even if Dr. Duggan's 95% "confidence interval" calculations could properly be interpreted as a confidence interval, which they cannot, the corrected calculations suggest it to be +/- \$10.03 million ($1.96 * \5.12 million) and a range from \$49.36 million to \$69.44 million. Given that Dr. Duggan's estimate of extrapolated differences is \$59.4 million, this confidence interval suggests a margin of error of roughly +/- 17% (+/- 10.03/59.4). This, however, likely understates the true error rate in his calculations, given the inflation detected in his extrapolations compared with claims data.

In conclusion, the error rate associated with Dr. Duggan's extrapolation can be examined directly through claims data without resorting to "confidence intervals". His own examination has demonstrated his extrapolations to be inaccurate. Furthermore, because of the unknown bias introduced by his use of a non-random sample with no correction, there is no statistical basis for the "confidence interval" calculation constructed by Dr. Duggan. It certainly provides no reliable basis to assess the error rates in his extrapolations. Finally, correcting some mathematical errors in Dr. Duggan's conceptually flawed "confidence interval" calculations boosts his error rate to at least +/- 17%.

Sincerely,



W. David Bradford, Ph. D.